

CLAIMS

1. A pharmaceutical composition comprising a photosensitizer agent conjugated to a compound selected from the group consisting of: bisphosphonates; 5 pyrophosphonates; thiobisphosphonates; and nitrobisphosphonates.

2. The composition of claim 1 wherein the photosensitizer agent is selected from the group consisting of chlorins, bacteriochlorins, phthalocyanines, porphyrins, purpurins, merocyanines, psoralens, benzoporphyrin derivatives (BPD), 10 porfimer sodium, delta-aminolevulinic acid, protoporphyrin, indocyanine green (ICG), methylene blue, toluidine blue, texaphyrins and any other agent that absorbs light in a range of 500 nm -1100 nm.

3. The composition of claim 1 wherein the compound is a bisphosphonate 15 of the formula

$$\begin{array}{c}
 \text{OH} \quad \text{R}_1 \quad \text{OH} \\
 | \quad \quad | \quad \quad | \\
 \text{O}=\text{P} \text{---} \text{C} \text{---} \text{P}=\text{O} \\
 | \quad \quad | \quad \quad | \\
 \text{OH} \quad \text{R}_2 \quad \text{OH}
 \end{array}$$

wherein R¹ is independently selected from the group consisting of: hydroxyl, an amino group, -CN, -NO₂, haloalkyl, heteroaryl, phenyl, alkyl, alkoxy, alkylthio, halo and alkyl-carbonyloxy; and wherein R² is independently selected from the group 20 consisting of: alkyl, aminoalkyl -CN, -NO₂, -NH₂, haloalkyl, heteroaryl, phenyl, alkyl, alkoxy, alkylthio, halo and alkyl-carbonyloxy.

4. The composition of claim 3 wherein R¹ is hydroxyl or an amino group and R² is alkyl or aminoalkyl. 25

5. The composition of claim 3 wherein the compound is selected from the group consisting of etidronate, tiludronate, clodronate, pamidronate, alendronate, risedronate and ibandronate.

30 6. The composition of claim 1 further conjugated to a target tissue

specific ligand.

7. The composition of claim 1 further conjugated to an imaging agent.

5 8. A method for destroying or impairing target cells involved in disease
of bone tissue in a mammalian subject comprising:

administering to the subject a therapeutically effective amount of the
composition of any one of claims 1 to 7, wherein said composition selectively binds
the target cells or target tissues involved in the disease of bone tissue; and

10 irradiating at least a portion of the subject with light at a wavelength or
waveband absorbed by said composition, wherein said light is provided by a light
source, and wherein said irradiation is at a relatively low fluence rate that results in
the activation of said composition; and

15 wherein said composition is cleared from non-target tissues of the subject
prior to said irradiation.

9. The method of claim 8, wherein said disease of bone tissue is a
metabolic bone disorder or bone metastases.

20 10. The method of claim 8 wherein said composition is conjugated to an
imaging agent.

11. The method of claim 10 further comprising the steps of performing a
nuclear medicine scan and imaging the target cells or target tissues to be destroyed or
25 impaired.

12. The method of claim 8, wherein said composition is conjugated to a
ligand that specifically binds to target cells or target tissues.

30 13. A method for destroying or impairing target cells involved in disease
of bone tissue in a mammalian subject comprising:

administering to the subject a therapeutically effective amount of a
composition comprising a photosensitizer agent conjugated to a compound selected

from the group consisting of: bisphosphonates; pyrophosphonates; thiobisphosphonates; and nitrobisphosphonates, wherein said composition selectively binds the target cells or target tissues involved in said disease of bone tissue; and

irradiating at least a portion of the subject with light at a wavelength absorbed by said composition, wherein said light is provided by a light source, and wherein said irradiation is at a relatively low fluence rate that results in the activation of said composition, wherein said composition is cleared from non-target tissues of the subject prior to said irradiation.

14. The method of claim 13, wherein said disease of bone is a metabolic bone disorder or bone metastases.

15. A method for treating a metabolic bone disorder or bone metastases in a mammalian subject comprising:

16. administering to the subject a therapeutically effective amount of a composition comprising

17. a photosensitizer agent selected from the group consisting of chlorins, bacteriochlorins, phthalocyanines, porphyrins, purpurins, merocyanines, psoralens, benzoporphyrin derivatives (BPD), porfimer sodium, delta-aminolevulinic acid, protoporphyrin, indocyanine green (ICG), methylene blue, toluidine blue, texaphyrins and any other agent that absorbs light in a range of 500 nm -1100 nm

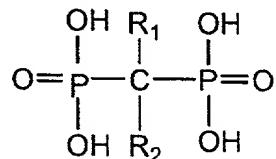
18. which is conjugated to a compound selected from the group consisting of: bisphosphonates; pyrophosphonates; thiobisphosphonates; and nitrobisphosphonates which selectively binds the target tissues or cells involved in the metabolic bone disorder or bone metastases and said composition is further conjugated to an imaging agent; and

19. performing a nuclear medicine scan;

20. imaging the target tissues or cells to be treated; and

21. irradiating at least a portion of the subject with light at a wavelength absorbed by said composition, wherein said light is provided by a light source, and wherein said irradiation is at a relatively low fluence rate that results in the activation of said composition, wherein said composition is cleared from non-target tissues of the subject prior to said irradiation.

16. A method for destroying or impairing target cells involved in disease of bone tissue in a mammalian subject according to claim 13 or 15, wherein said compound is a bisphosphonate of the formula



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wherein R^1 is independently selected from the group consisting of: hydroxyl, an amino group, $-\text{CN}$, $-\text{NO}_2$, haloalkyl, heteroaryl, phenyl, alkyl, alkoxy, alkylthio, halo and alkyl-carbonyloxy; and wherein R^2 is independently selected from the group consisting of: alkyl, aminoalkyl $-\text{CN}$, $-\text{NO}_2$, $-\text{NH}_2$, haloalkyl, heteroaryl, phenyl, alkyl, alkoxy, alkylthio, halo and alkyl-carbonyloxy.

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17. The method according to claim 13 or 15, wherein R^1 is hydroxyl or an amino group and R^2 is alkyl or aminoalkyl.

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18. A method according to claim 13 or 15, wherein the compound is selected from the group consisting of etidronate, tiludronate, clodronate, pamidronate, alendronate, risedronate and ibandronate.

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19. A method according to claim 13 or 15, wherein the composition is conjugated to a target tissue specific ligand or an imaging agent.

20. A method for destroying or impairing target cells involved in disease of bone tissue in a mammalian subject comprising:

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administering to the subject a therapeutically effective amount of a composition comprising a photosensitizer agent, wherein said agent is selected from the group consisting of chlorins, bacteriochlorins, phthalocyanines, porphyrins, purpurins, merocyanines, psoralens, benzoporphyrin derivatives (BPD), porfimer sodium, delta-aminolevulinic acid, protoporphyrin, indocyanine green (ICG), methylene blue, toluidine blue, texaphyrins and any other agent that absorbs light in a range of 600 nm -1100 nm, and wherein said agent is conjugated to a compound

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selected from the group consisting of: bisphosphonates; pyrophosphonates; thiobisphosphonates; and nitrobisphosphonates; and wherein said composition selectively binds the target cells or target tissues involved in said disease of bone tissue; and

5 irradiating at least a portion of the subject with light at a wavelength absorbed by said composition, wherein said light is provided by a light source, and wherein said irradiation is at a relatively low fluence rate that results in the activation of said composition; and

10 wherein said composition is cleared from non-target cells or non-target tissues of the subject prior to said irradiation.

21. The method of claim 20, wherein said disease of bone tissue is a metabolic bone disorder or bone metastases.

15 22. The method of any one of claims 8-21, wherein said fluence rate results in the irradiating of said subject with a total fluence of irradiation delivered either internally or from an external light source at a range of about between 30 Joules/cm² to 25,000 Joules/cm².

20 23. The method of claim 22, wherein said range is between 100 Joules/cm² to 20,000 Joules/cm².

24. The method of claim 23, wherein said range is between 500 Joules/cm² to 10,000 Joules/cm².